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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,545	11/15/2000	Russell N. Van Gelder	LBS-002COB	4526

25003 7590 05/07/2003

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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/07/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/713,545	Applicant(s) Van Gelder et al.
	Examiner William Sandals	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Feb 19, 2003* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see NOTE below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☒ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: *42-54*

Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .

10. ☐ Other:

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09/713,545			

EXAMINER	
William Sandals	
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1636	18

DATE MAILED:

Please find below a communication from the EXAMINER in charge of this application

Commissioner of Patents

1. Claims 42-54 are pending. Claims 42-54 stand rejected as obvious under 35 USC 103 over US 5,112,734 (Kramer et al.) in view of US 5,043,272 (Hartley), and further in view of US 5,466,788 (Alquist et al.) and Kwoh et al.

2. Arguments in Paper No. 17, page 2, Filed February 19, 2003, regarding the rejection under 35 USC 103 assert that Kramer et al. did not teach "linearly amplified RNA copies" nor "relative representation of the specific nucleic acid messages within the sample".

Kramer et al. teach the amplification of mRNA (messages) by producing a cDNA from mRNA, where the cDNA has been modified to include an RNA polymerase promoter. An RNA polymerase is then used to produce multiple copies of the cDNA (amplification). This method is

the linear method used in the instant application. Therefore, the term "linear amplification" applies to the method of Kramer et al.

Kramer et al. teach the amplification of a single mRNA, and as stated in the rejection, Kramer et al. does not teach a multigene expression profile. However, Kramer et al. teaches at column 4, lines 43-48 that "the replicated RNA is detected as indicative of the presence or the amount of target sequence". This statement is clear recognition by Kramer et al. that "relative representation" of mRNAs in the sample directly relates to the "relative amounts" of each amplified mRNA. Therefore, the arguments regarding Kramer et al. are not found convincing.

3. Arguments in Paper No. 17, page 2, assert that Hartley et al. teach amplification using random primers, and do not teach linear amplification, nor that the amplified mRNA's are present in an abundance which reflects the relative representation of specific mRNAs in the sample.

Hartley teach that it is obvious to produce a library of mRNAs (messages) which are then amplified from a sample containing mRNAs. The relative abundance of the amplified mRNAs of Hartley is not necessarily related to the abundance of the mRNAs in the sample. However, the relative abundance is the same in the method of Kramer et al. when modified with the library of Hartley.

As proof of the principle of the production of amplified mRNAs which have a relative representation, WO 89/06700 (Miller et al.) recites at the summary a method of amplification of mRNA (messages) by producing a cDNA from mRNA, where the cDNA has been modified to

include an RNA polymerase promoter, then an RNA polymerase is used to produce multiple transcripts (copies) of the cDNA (amplification) (this method of amplification uses the RNA polymerase promoter to produce linear amplification as recited in the instant application, as does the method of amplification recited in Kramer et al.). WO 89/06700 recites at page 15, lines 26-30 that the method produces amplified RNA transcripts in proportion to the amount of mRNA originally present in the sample.

4. Arguments in Paper No. 17, page 3, assert that it would not have been obvious to combine the method of Kramer et al. with the method of Hartley.

It is obvious to modify the method of amplifying the one, or a few, mRNAs as taught by Kramer et al. with the method of making a library of mRNAs for amplification as taught by Hartley for the expected benefit of being able to detect specific nucleic acids which are present in a "library" of mRNAs in a biological sample.

5. Arguments in Paper No. 17, page 3, assert that US 5,466,788 (Alquist et al.) does not teach the production of multiple genes one at a time.

This is not a limitation of the instant claims. Therefore, the argument is not directed to the subject matter under rejection.

6. Arguments in Paper No. 17, page 3, assert that Alquist et al. teaches at column 2:32-33, that the (+) strand amplified mRNAs outnumber the (-) strand amplified mRNAs.

While this observation has some biological interest, column 2 is in the "background" section, and does not rebut the relevant teachings of Alquist et al. that describe the advantages of

using aRNA in methods of amplification of RNAs as recited in the final rejection. The argument is therefore not found convincing.

7. Arguments in Paper No. 17, page 3, assert that the references alone or in combination do not teach the instant claimed "collection of linearly amplified specific messages (mRNAs) within the sample".

As stated above, both Kramer et al. and Hartley teach the desirability of detecting mRNAs in a sample. The method of Kramer et al. is a method of linear amplification for detection of specific mRNAs in a sample. The method of Hartley is a method of amplification of libraries of mRNAs for detecting the specific mRNAs represented in the sample. The obvious combination of Kramer et al. and Hartley produces the instant claimed "collection of linearly amplified specific messages (mRNAs) within the sample". Therefore, the argument is not found convincing.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William Sandals whose telephone number is (703) 305-1982. The examiner can normally be reached on Monday through Thursday from 8:30 AM to 7:00 PM.

May 1, 2003

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